REMARKS

Claims 54 to 56, and 59 to 66 are pending in this application. Applicants have amended claims 54 and 71 and canceled claims 57, 58, and 67 to 73, without prejudice to applicants' right to pursue any one or more of these claims in a subsequent continuation application. These amendments add no new matter. In particular, applicants have amended the claims to remove references to adenosine and to focus the invention on the use of adenosine analogs to enhance the condition of unbroken skin without increasing dermal cell proliferation, and compositions comprising adenosine analogs and an angiogenesis factor. These concepts were already in the claims, and are described throughout the application.

Claim Objections

The Office Action notes that claims 57 and 58 are substantial duplicates of claims 55 and 56. Applicants disagree, because claims 57 and 58 relate to adenosine, and claims 55 and 56 relate to adenosine **analogs**, but by the present amendment, applicants have cancelled claims 57 and 58 rendering this rejection moot.

Double Patenting

Claims 55-59 have been rejected under U.S.C. § 101 as allegedly claiming the same invention as that of claims 1 and 4 of prior U.S. Patent No. 6,423,327 ("the '327 patent").

Applicants respectfully disagree, because the pending claims now focus on the use of adenosine **analogs**, whereas the claims in the '327 patent recite methods using adenosine, not adenosine analogs. Thus, the present claims do not claim the same invention as any of the claims in the '327 patent.

Claims 54-73 have been rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-10 of U.S. Patent No. 6,645,513 ("the '513 patent"). The Office Action admits that "the conflicting claims are not identical," but alleges that "they are not patentably distinct from each other because both the sets of claims are directed to a method of enhancing the skin condition by topically applying

adenosine or adenosine analog in an amount effective to enhance the condition of the skin" (at page 3). Applicants again respectfully disagree, because the '513 patent does not recite the use of adenosine analogs, and all pending claims in the present application recite adenosine analogs. Thus, the present claims do not recite the same invention, or even an obvious variation of the invention, claimed in the '513 patent.

35 U.S.C. § 102

Claims 54-62, 65, 67, and 69 have been rejected under 35 U.S.C. 102(e) as being allegedly anticipated by U.S. Patent No. 5,998,423 to Manneth et all ("the '423 patent"). Applicants respectfully disagree and traverse this rejection for the following reasons.

According to the Office Action, the '423 patent describes compositions comprising adenosine, cyclohexyladenosine, or cyclopentyladenosine and their use for the modulation of melanin production in the skin and hair and in enhancing the tanning process and providing protection for the skin against UV radiation (see col. 1, lines 7-13; col. 2, lines 44-63; col. 5, lines 10-18). The Office Action assumes, without any factual support, that "enhancing the tanning process on the skin, taught by '423, reads on the enhancing the condition for non-diseased skin" (Office Action at page 4). Applicants disagree, because nowhere does the '423 patent state that its compositions or methods reduce one or more of wrinkling, roughness, dryness, or laxity of the skin without increasing proliferation of dermal cells in the skin. Instead, the '423 patent merely describes that its methods can be used to modulate melanin production and protect against UV rays. In fact, the '423 patent does not even use the terms wrinkle (or wrinkling), roughness, dryness, or laxity anywhere in its text (based on an electronic word search). Thus, enhancing the tanning process (i.e., getting a better tan) and protecting the skin against UV rays is not the same as enhancing the condition of unbroken skin as presently claimed.

Furthermore, the Office Action alleges that "with respect to claimed amounts of adenosine agonists, '423 discloses preferred amounts of adenosine receptor antagonists (which is same as adenosine agonists), in the range of 100nM or 10nM, which is within the claimed range

(col. 3, lies [sic, lines] 8-12 and col. 4, lines 7-17). Applicants again respectfully disagree, because the numbers recited in the '423 patent at column 4, lines 7 to 17 are in fact K_i values, which are measures of activity level with respect to an adenosine receptor binding assay, and not concentrations to be administered.

Next, the Office Action alleges that the '423 patent does not show that the adenosine agonists show any increase in cell proliferation, and thus assumes that this is a fact. Applicants submit that the '423 patent is silent on the issue, and thus the Office cannot merely assume that the '423 patent methods do not cause an increase in dermal cell proliferation. To the contrary, the Office Action provides no evidence whatsoever to support the rejection. Unless the Examiner provides some evidence to support the conjecture that the '423 patent compounds will not increase cell proliferation (which as far as applicants understand has nothing to do with improving a tan), the burden of proof does not shift to applicants.

As the Examiner is no doubt aware, "[a]nticipation under Section 102 requires 'the presence in a single prior art disclosure of all elements of a claimed invention arranged as in that claim,'" Carella v. Starlight Archery and Pro Line Co., 804 F.2d 135, 138 (Fed. Cir. 1986), and "[t]he identical invention must be shown in as complete detail as is contained in the ... claim," Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The present Office Action does not meet these requirements, and thus, for all of these reasons, applicants submit that the '423 patent fails to anticipate the instant claims. As a result, applicants request that the Examiner reconsider and withdraw this rejection.

Next, claims 54, 59-61, and 66 have been rejected under 35 U.S.C. 102(e) as being allegedly anticipated by U.S. Patent No. 5,256,649 to Le Fur et al ("the '649 patent"). Applicants respectfully disagree and traverse this rejection for the following reasons.

According to the Office Action, the '649 patent discloses a cosmetic composition for treating aging skin that includes ATP or an ATP generating system and cosmetic additives such as emollients and humectants. The Office Action also states that the '649 patent recites that the composition slows down aging by maintaining optimum fluidity of the skin cell membrane and improves the condition of the skin, but does not mention cell proliferation. Again, the Examiner

merely alleges that silence in the patent indicates that the recited formulations do not increase cell proliferation. Applicants disagree, and note that the Examiner has no factual evidence or support for his conclusions.

More importantly, the '649 patent does not disclose the same concentrations of ATP as recited in applicants' amended claims to the use of adenosine analogs. The '649 patent recites percentages of ATP of 0.045 to 4.5 percent by weight of the composition. Given ATP's molecular weight, this concentration range is far higher than applicants' claimed range of concentrations. Applicants' highest claimed concentration is now 10^{-4} M, which corresponds to an ATP concentration of about 0.006 percent. This upper concentration of 0.006 percent is far lower that the 0.045 percent lower level that the '649 patent discloses, and there is no suggestion in the '649 patent that a lower concentration of ATP could work in the claimed methods.

Based on these reasons, the '649 patent does not anticipate the presently amended claims, and applicants request that the Examiner reconsider and withdraw this rejection.

35 U.S.C. § 103

Claims 55-58, 67, 68, and 70 have been rejected as being allegedly unpatentable over the '649 patent. Applicants traverse for the reasons discussed above and for the following reasons.

The Office Action notes that while the '649 patent "does not specify the amounts of ATP in terms of molar percentages, '649 suggests ATP at 0.45 to 4.5% (col. 3 table)," and concludes that "it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to choose an optimum amount of ATP in the cosmetic composition of '649 with an expectation to achieve the desired effect of combating the external factors so as to prevent premature aging of the skin because '649 suggests that ATP or ATP generating system in the composition slows down aging by maintaining optimum fluidity of the skin cell membrane and improving the condition of the skin (col. 5) (Office Action, at pages 5-6)."

Applicants respectfully disagree. As noted above, the concentration range of the '649 patent now varies from the claimed concentration range by about an order of magnitude, and there is simply no suggestion in the '649 patent that either the claimed methods or the '649

methods would work at such low concentrations as applicants are now claiming. Furthermore, as best understood by applicants, the purpose of the ATP in the '649 patent is to supply energy for betaine to generate ademetionine, which in turn has the anti-aging effect (see, e.g., col. 1, lines 36-43 and lines 48-49). This is an intracellular process intended to increase membrane fluidity. These intracellular actions of the betaine/ATP mixture are unrelated to the ATP receptor activity addressed by applicants' claimed methods using applicants' claimed low concentrations of adenosine analogs. Applicants' claimed methods are believed to stimulate receptor-mediated physiological responses on the skin cells to enhance protein synthesis, cell size, etc., to enhance the condition of the skin. These are entirely different effects than the betaine/ATP mixture proposed in the '649 patent to increase membrane fluidity.

Thus, applicants submit that it would not have been obvious to one of skill in the art upon reading the '649 patent to lower the concentration of the ATP by almost an order of magnitude, much less to carry out the presently claimed methods. Based on these reasons, applicants request the Examiner to reconsider and withdraw this rejection.

Next, claims 62, 71, 72, and 73 have been rejected as being allegedly unpatentable over the '649 patent and further in view of U.S. Patent No. 5,770,582 to von Borstel et al. ("the '582 patent"). Applicants have cancelled claims 71 to 73, without prejudice, thereby rendering this rejection moot with respect to these claims. With respect to claim 62, that claim depends from claim 54, and is thus patentable for at least the same reasons as claim 54 as discussed above.

Claims 71, 72, and 73 have been rejected as being allegedly unpatentable over the '423 patent in view of the '582 patent. Applicants have cancelled claims 71 to 73, without prejudice, thereby rendering this rejection moot.

Claims 63 and 64 have been rejected as being allegedly unpatentable over the '423 patent or the '649 patent in view of U.S. Patent No. 5,785,978 to Porter. Applicants submit that claims 63 and 64 are patentable for at least the same reasons that claim 54, from which these claims depend, is patentable.

CONCLUSION

Applicants request that the Examiner reconsider and withdraw the rejections of the pending claims, and send a Notice of Allowance.

No excess claim fees are required. Applicants enclose a $510 check for the extension fee along with a Petition for Extension of Time for Three Months. Please apply any other charges or credits to deposit account 06-1050, referring to attorney docket 07917-045004.

Respectfully submitted,

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